Amendments to the Specification:

Please replace the paragraph beginning at page 2, line 29 of the specification with the following amended paragraph:

In one embodiment, a NIP2b, NIP2cL, or NIP2cS nucleic acid molecule of the invention is at least 59%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98%, or more identical to the nucleotide sequence (e.g., to the entire length of the nucleotide sequence) shown in SEQ ID NO:1, 3, 4, 6, 7, or 9 ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a complement thereof.

Please replace the paragraph beginning at page 3, line 23 of the specification with the following amended paragraph:

In another embodiment, a NIP2b, NIP2cL, and NIP2cS nucleic acid molecule includes a nucleotide sequence encoding a protein having an amino acid sequence sufficiently homologous to the amino acid sequence of SEQ ID NO:2, 5, or 8 ~~or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In a preferred embodiment, a NIP2b, NIP2cL, and NIP2cS nucleic acid molecule includes a nucleotide sequence encoding a protein having an amino acid sequence at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or more homologous to the entire length of the amino acid sequence of SEQ ID NO:2, 5, or 8 ~~or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~.

Please replace the paragraph beginning at page 3, line 33 of the specification with the following amended paragraph:

In another preferred embodiment, an isolated nucleic acid molecule encodes the amino acid sequence of human NIP2b, NIP2cL, and NIP2cS. In yet another preferred embodiment, the nucleic acid molecule includes a nucleotide sequence encoding a protein having the amino acid sequence of SEQ ID NO:2, 5, or 8 ~~or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In yet another preferred embodiment, the nucleic acid molecule is at least 461, 535, or 3225 nucleotides in length. In a

further preferred embodiment, the nucleic acid molecule is at least 461, 535, or 3225 nucleotides in length and encodes a protein having a NIP2b, NIP2cL, and NIP2cS activity (as described herein).

Please replace the paragraph beginning at page 4, line 4 of the specification with the following amended paragraph:

Another embodiment of the invention features nucleic acid molecules, preferably NIP2b, NIP2cL, and NIP2cS nucleic acid molecules, which specifically detect NIP2b, NIP2cL, and NIP2cS nucleic acid molecules relative to nucleic acid molecules encoding non-NIP2b, non-NIP2cL, and non-NIP2cS proteins. For example, in one embodiment, such a nucleic acid molecule is at least 300-350, 350-400, 400-450, 461, 461-500, 535, 535-600 or more nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, 4, or 7, ~~the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a complement thereof.

Please replace the paragraph beginning at page 4, line 27 of the specification with the following amended paragraph:

In other preferred embodiments, the nucleic acid molecule encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, 5, or 8 ~~or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, 3, 4, 6, 7, or 9 under stringent conditions.

Please replace the paragraph beginning at page 5, line 7 of the specification with the following amended paragraph:

Another aspect of this invention features isolated or recombinant NIP2b, NIP2cL, and NIP2cS proteins and polypeptides. In one embodiment, the isolated protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one transmembrane domain. In a preferred embodiment, the isolated protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one calcium binding domain. In yet another preferred embodiment, the isolated protein,

preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one "4 transmembrane segment integral membrane protein domain". In a preferred embodiment, the protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one transmembrane domain and has an amino acid sequence at least about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or more homologous to the amino acid sequence of SEQ ID NO:2, 5, or 8 ~~or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In another embodiment, the protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one calcium-binding domain and has an amino acid sequence at least about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or more homologous to the amino acid sequence of SEQ ID NO:2, 5, or 8 ~~or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In yet another preferred embodiment, the protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one "4 transmembrane segment integral membrane protein domain" and has an amino acid sequence at least about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or more homologous to the amino acid sequence of SEQ ID NO:2, 5, or 8 ~~or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In another preferred embodiment, the protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one transmembrane domain and plays a role in apoptosis or programmed cell death. In another embodiment, the protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one calcium-binding domain and plays a role in apoptosis or programmed cell death. In yet another preferred embodiment, the protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one "4 transmembrane segment integral membrane protein domain" and plays a role in apoptosis or programmed cell death. In yet another preferred embodiment, the protein, preferably a NIP2b, NIP2cL, and NIP2cS protein, includes at least one transmembrane domain and is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9. In another embodiment, the protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one calcium-binding domain and is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9. In yet another preferred embodiment,

the protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, includes at least one "4 transmembrane segment integral membrane protein domain" and is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9.

Please replace the paragraph beginning at page 6, line 11 of the specification with the following amended paragraph:

In another embodiment, the invention features fragments of the protein having the amino acid sequence of SEQ ID NO:2, 5, or 8, wherein the fragment comprises at least 15 amino acids (e.g., contiguous amino acids) of the amino acid sequence of SEQ ID NO:2, 5, or 8 ~~or an amino acid sequence encoded by the DNA insert of the plasmid deposited with the ATCC as Accession Number_____~~. In another embodiment, the protein, preferably a NIP2b, NIP2cL, or NIP2cS protein, has the amino acid sequence of SEQ ID NO:2, 5, or 8, respectively.

Please replace the paragraph beginning at page 13, line 12 of the specification with the following amended paragraph:

The nucleotide sequence of the isolated human NIP2b cDNA and the predicted amino acid sequence of the human NIP2b polypeptide are shown in Figure 1 and in SEQ ID NOs:1 and 2, respectively. ~~A plasmid containing the nucleotide sequence encoding human NIP2b was deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on_____ and assigned Accession Number_____. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112~~.

Please replace the paragraph beginning at page 5, line 31 of the specification with the following amended paragraph:

The nucleotide sequence of the isolated human NIP2cL cDNA and the predicted amino acid sequence of the human NIP2cL polypeptide are shown in Figure 2 and in SEQ ID NOs:4 and 5, respectively. ~~A plasmid containing the nucleotide sequence encoding human NIP2cL was deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on _____ and assigned Accession Number _____. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.~~

Please replace the paragraph beginning at page 14, line 14 of the specification with the following amended paragraph:

The nucleotide sequence of the isolated human NIP2cS cDNA and the predicted amino acid sequence of the human NIP2cS polypeptide are shown in Figure 3 and in SEQ ID NOs:7 and 8, respectively. ~~A plasmid containing the nucleotide sequence encoding human NIP2cS was deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on _____ and assigned Accession Number _____. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.~~

Please replace the paragraph beginning at page 15, line 27 of the specification with the following amended paragraph:

A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9,~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion thereof, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or portion of the nucleic acid sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as~~

~~Accession Number _____~~, as a hybridization probe, NIP2b, NIP2cL, and NIP2cS nucleic acid molecules can be isolated using standard hybridization and cloning techniques (e.g., as described in Sambrook, J., Fritsh, E. F., and Maniatis, T. *Molecular Cloning: A Laboratory Manual. 2nd. ed., Cold Spring Harbor Laboratory,* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

Please replace the paragraph beginning at page 16, line 1 of the specification with the following amended paragraph:

Moreover, a nucleic acid molecule encompassing all or a portion of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ can be isolated by the polymerase chain reaction (PCR) using synthetic oligonucleotide primers designed based upon the sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~.

Please replace the paragraph beginning at page 16, line 35 of the specification with the following amended paragraph:

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, or ~~9, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ , or a portion of any of these nucleotide sequences. A nucleic acid molecule which is complementary to the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, is one which is sufficiently complementary to the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, such that it can hybridize to the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, thereby forming a stable duplex.

Please replace the paragraph beginning at page 17, line 9 of the specification with the following amended paragraph:

In still another preferred embodiment, an isolated nucleic acid molecule of the present invention comprises a nucleotide sequence which is at least about 59%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or more homologous to the entire length of the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the entire length of the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion of any of these nucleotide sequences.

Please replace the paragraph beginning at page 17, line 15 of the specification with the following amended paragraph:

Moreover, the nucleic acid molecule of the invention can comprise only a portion of the nucleic acid sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, for example, a fragment which can be used as a probe or primer or a fragment encoding a portion of a NIP2b, NIP2cL, and NIP2cS protein, e.g., a biologically active portion of a NIP2b, NIP2cL, and NIP2cS protein. The nucleotide sequence determined from the cloning of the NIP2b, NIP2cL, and NIP2cS gene allows for the generation of probes and primers designed for use in identifying and/or cloning other NIP2b, NIP2cL, and NIP2cS family members, as well as NIP2b, NIP2cL, and NIP2cS homologues from other species. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12 or 15, preferably about 20 or 25, more preferably about 30, 35, 40, 45, 50, 55, 60, 65, or 75 consecutive nucleotides of a sense sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, of an anti-sense sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or of a naturally occurring allelic variant or mutant of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the~~

~~plasmid deposited with ATCC as Accession Number _____~~. In an exemplary embodiment, a nucleic acid molecule of the present invention comprises a nucleotide sequence which is greater than 300-350, 350-400, 400-450, 461, 462-500, 535, 536-550, 550-600, 600-650, 650-700, 700-750, 750-800, 800-850, 850-900, 900-950, 950-1000, or more nucleotides in length and hybridizes under stringent hybridization conditions to a nucleic acid molecule of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~.

Please replace the paragraph beginning at page 18, line 12 of the specification with the following amended paragraph:

A nucleic acid fragment encoding a "biologically active portion of a NIP2b, NIP2cL, and NIP2cS protein" can be prepared by isolating a portion of the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, which encodes a polypeptide having a NIP2b, NIP2cL, and NIP2cS biological activity (the biological activities of the NIP2b, NIP2cL, and NIP2cS proteins are described herein), expressing the encoded portion of the NIP2b, NIP2cL, and NIP2cS protein (e.g., by recombinant expression *in vitro*) and assessing the activity of the encoded portion of the NIP2b, NIP2cL, and NIP2cS protein.

Please replace the paragraph beginning at page 14, line 14 of the specification with the following amended paragraph:

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, due to degeneracy of the genetic code and thus encode the same NIP2b, NIP2cL, and NIP2cS proteins as those encoded by the nucleotide sequence shown in SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a protein having an amino acid sequence shown in SEQ ID NO:2, 5, or 8.

Please replace the paragraph beginning at page 18, line 29 of the specification with the following amended paragraph:

In addition to the NIP2b, NIP2cL, and NIP2cS nucleotide sequences shown in SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of the NIP2b, NIP2cL, and NIP2cS proteins may exist within a population (e.g., the human population). Such genetic polymorphism in the NIP2b, NIP2cL, and NIP2cS genes may exist among individuals within a population due to natural allelic variation. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules which include an open reading frame encoding a NIP2b, NIP2cL, and NIP2cS protein, preferably a mammalian NIP2b, NIP2cL, and NIP2cS protein, and can further include non-coding regulatory sequences, and introns.

Please replace the paragraph beginning at page 19, line 24 of the specification with the following amended paragraph:

Moreover, nucleic acid molecules encoding other NIP2b, NIP2cL, and NIP2cS family members and, thus, which have a nucleotide sequence which differs from the NIP2b, NIP2cL, and NIP2cS sequences of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ are intended to be within the scope of the invention. For example, another NIP2b, NIP2cL, and NIP2cS cDNA can be identified based on the nucleotide sequence of human NIP2b, NIP2cL, and NIP2cS. Moreover, nucleic acid molecules encoding NIP2b, NIP2cL, and NIP2cS proteins from different species, and which, thus, have a nucleotide sequence which differs from the NIP2b, NIP2cL, and NIP2cS sequences of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ are intended to be within the scope of the invention. For example, a mouse NIP2b, NIP2cL, and NIP2cS cDNA can be identified based on the nucleotide sequence of a human NIP2b, NIP2cL, and NIP2cS.

Please replace the paragraph beginning at page 20, line 7 of the specification with the following amended paragraph:

Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 15, 20, 25, 30 or more nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. In other embodiment, the nucleic acid is at least 30, 50, 100, 150, 200, 250, 300, 308, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, or 950 nucleotides in length. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other. Preferably, the conditions are such that sequences at least about 70%, more preferably at least about 80%, even more preferably at least about 85% or 90% homologous to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 50°C, preferably at 55°C, more preferably at 60°C, and even more preferably at 65°C. Preferably, an isolated nucleic acid molecule of the invention that hybridizes under stringent conditions to the sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9 corresponds to a naturally-occurring nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein).

Please replace the paragraph beginning at page 20, line 29 of the specification with the following amended paragraph:

In addition to naturally-occurring allelic variants of the NIP2b, NIP2cL, and NIP2cS sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, thereby leading to changes in the amino acid sequence of the encoded NIP2b, NIP2cL, and NIP2cS proteins, without altering the functional ability of the NIP2b, NIP2cL, and

NIP2cS proteins. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of NIP2b, NIP2cL, and NIP2cS (e.g., the sequence of SEQ ID NO:2, 5, or 8) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are conserved among the NIP2b, NIP2cL, and NIP2cS proteins of the present invention, are predicted to be particularly unamenable to alteration. Furthermore, additional amino acid residues that are conserved between the NIP2b, NIP2cL, and NIP2cS proteins of the present invention and other members of the NIP2 family are not likely to be amenable to alteration.

Please replace the paragraph beginning at page 21, line 16 of the specification with the following amended paragraph:

An isolated nucleic acid molecule encoding a NIP2b, NIP2cL, and NIP2cS protein homologous to the protein of SEQ ID NO:2, 5, or 8 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced into SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains

(e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in a NIP2b, NIP2cL, and NIP2cS protein is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a NIP2b, NIP2cL, and NIP2cS coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for NIP2b, NIP2cL, and NIP2cS biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

Please replace the paragraph beginning at page 24, line 6 of the specification with the following amended paragraph:

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave NIP2b, NIP2cL, and NIP2cS mRNA transcripts to thereby inhibit translation of NIP2b, NIP2cL, and NIP2cS mRNA. A ribozyme having specificity for a NIP2b, NIP2cL, and NIP2cS-encoding nucleic acid can be designed based upon the nucleotide sequence of a NIP2b, NIP2cL, and NIP2cS cDNA disclosed herein (i.e., SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a NIP2b, NIP2cL, and NIP2cS-encoding mRNA. See, e.g., Cech et al. U.S. Patent No. 4,987,071; and Cech et al. U.S. Patent No. 5,116,742. Alternatively, NIP2b, NIP2cL, and NIP2cS mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel, D. and Szostak, J.W. (1993) *Science* 261:1411-1418.

Please replace the paragraph beginning at page 41, line 30 of the specification with the following amended paragraph:

A transgenic animal of the invention can be created by introducing a NIP2b, NIP2cL, and NIP2cS-encoding nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The NIP2b, NIP2cL, and NIP2cS cDNA sequence of SEQ ID NO:1, 4, or 7 can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of a human NIP2b, NIP2cL, and NIP2cS gene, such as a mouse or rat NIP2b, NIP2cL, and NIP2cS gene, can be used as a transgene. Alternatively, a NIP2b, NIP2cL, and NIP2cS gene homologue, such as another NIP2 family member, can be isolated based on hybridization to the NIP2b, NIP2cL, and NIP2cS cDNA sequences of SEQ ID NO:1, 3, 4, 6, 7, ~~or 9, or the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~ (described further in subsection I above) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to a NIP2b, NIP2cL, and NIP2cS transgene to direct expression of a NIP2b, NIP2cL, and NIP2cS protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, both by Leder et al., U.S. Patent No. 4,873,191 by Wagner et al. and in Hogan, B., *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of a NIP2b, NIP2cL, and NIP2cS transgene in its genome and/or expression of NIP2b, NIP2cL, and NIP2cS mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding a NIP2b, NIP2cL, and NIP2cS protein can further be bred to other transgenic animals carrying other transgenes.

Please replace the paragraph beginning at page 59, line 18 of the specification with the following amended paragraph:

An exemplary method for detecting the presence or absence of NIP2b, NIP2cL, and NIP2cS protein or nucleic acid in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting NIP2b, NIP2cL, and NIP2cS protein or nucleic acid (e.g., mRNA, genomic DNA) that encodes NIP2b, NIP2cL, and NIP2cS protein such that the presence of NIP2b, NIP2cL, and NIP2cS protein or nucleic acid is detected in the biological sample. A preferred agent for detecting NIP2b, NIP2cL, and NIP2cS mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to NIP2b, NIP2cL, and NIP2cS mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length NIP2b, NIP2cL, and NIP2cS nucleic acid, such as the nucleic acid of SEQ ID NO:1, 3, 4, 6, 7, or 9, ~~or the DNA insert of the plasmid deposited with ATCC as Accession Number _____~~, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to NIP2b, NIP2cL, and NIP2cS mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

Please replace the paragraph beginning at page 72, line 10 of the specification with the following amended paragraph:

The nucleotide sequence encoding the human NIP2b protein is shown in Figure 1 and is set forth as SEQ ID NO:1. The full length protein encoded by this nucleic acid comprises about 371 amino acids and has the amino acid sequence shown in Figure 1 and set forth as SEQ ID NO:2. The coding region (open reading frame) of SEQ ID NO:1 is set forth as SEQ ID NO:3. ~~Clone NIP2b, comprising the entire coding region of human NIP2b was deposited with the American Type Culture Collection (ATCC®), 10801 University Boulevard, Manassas, VA 20110-2209, on _____, and assigned Accession No. _____.~~

Please replace the paragraph beginning at page 72, line 18 of the specification with the following amended paragraph:

The nucleotide sequence encoding the human NIP2cL protein is shown in Figure 2 and is set forth as SEQ ID NO:4. The full length protein encoded by this nucleic acid comprises about 322 amino acids and has the amino acid sequence shown in Figure 2 and set forth as SEQ ID NO:5. The coding region (open reading frame) of SEQ ID NO:4 is set forth as SEQ ID NO:6. ~~Clone NIP2cL, comprising the entire coding region of human NIP2cL was deposited with the American Type Culture Collection (ATCC®), 10801 University Boulevard, Manassas, VA 20110-2209, on _____, and assigned Accession No. _____.~~

Please replace the paragraph beginning at page 72, line 26 of the specification with the following amended paragraph:

The nucleotide sequence encoding the human NIP2cS protein is shown in Figure 3 and is set forth as SEQ ID NO:7. The full length protein encoded by this nucleic acid comprises about 126 amino acids and has the amino acid sequence shown in Figure 3 and set forth as SEQ ID NO:8. The coding region (open reading frame) of SEQ ID NO:7 is set forth as SEQ ID NO:9. ~~Clone NIP2cS, comprising the entire coding region of human NIP2cS was deposited with the American Type Culture Collection (ATCC®), 10801 University Boulevard, Manassas, VA 20110-2209, on _____, and assigned Accession No. _____.~~